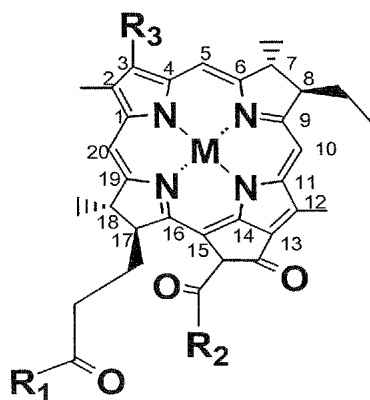


**AMENDMENTS TO THE CLAIMS:**

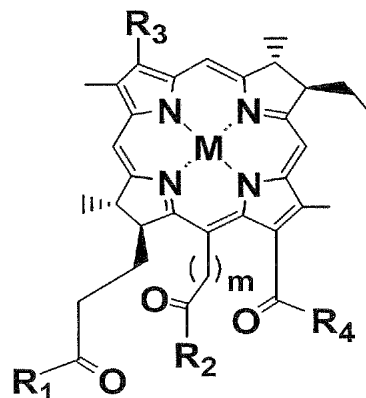
This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1. (Currently Amended) A bacteriochlorophyll ~~derivative compound~~ containing at least one, ~~preferably two or three,~~ negatively charged ~~groups~~ group or acidic ~~groups~~ group that ~~are~~ is converted to negatively charged groups at the physiological pH, of the formula I or II:



(I)



(II)

wherein

M represents 2H or a metal atom selected from the group consisting of divalent Pd, Pt, Co, Sn, Ni, Cu, Zn and Mn, or trivalent Fe, Mn and Cr;

R<sub>1</sub>, R<sub>2</sub>, and R<sub>4</sub> each independently is Y- R<sub>5</sub>;

Y is O, S or -NR<sub>6</sub>;

R<sub>3</sub> is selected from the group consisting of -CH=CH<sub>2</sub>, -C(=O)-CH<sub>3</sub>, -C(=O)-H, -CH=NR<sub>7</sub>, -C(CH<sub>3</sub>)=NR<sub>7</sub>, -CH<sub>2</sub>-OR<sub>7</sub>, -CH<sub>2</sub>-SR<sub>7</sub>, -CH<sub>2</sub>-NR<sub>7</sub>R'<sub>7</sub>, -CH(CH<sub>3</sub>)-OR<sub>7</sub>, -CH(CH<sub>3</sub>)-SR<sub>7</sub>, -CH(CH<sub>3</sub>)-NR<sub>7</sub>R'<sub>7</sub>, -CH(CH<sub>3</sub>)Hal, -CH<sub>2</sub>-Hal, -CH<sub>2</sub>-R<sub>7</sub>, -CH=CR<sub>7</sub>R'<sub>7</sub>, -C(CH<sub>3</sub>)=CR<sub>7</sub>R'<sub>7</sub>, -CH=CR<sub>7</sub>Hal, -C(CH<sub>3</sub>)=CR<sub>7</sub>Hal, and -C≡CR<sub>7</sub>;

R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R'<sub>7</sub> each independently is H or selected from the group consisting of:

(a) C<sub>1</sub>-C<sub>25</sub> hydrocarbyl optionally containing one or more heteroatoms selected from the group consisting of -O, S and N, carbocyclic or heterocyclic moieties such as pyridyl, and/or optionally substituted by one or more functional groups selected from the group consisting of halogen, oxo, OH, SH, CHO, NH<sub>2</sub>, CONH<sub>2</sub>, a negatively charged group, and an acidic group that is converted to a negatively charged group at the physiological pH;

(b) a residue of an amino acid, a peptide or of a protein;  
and

(c) when Y is O or S, R<sub>5</sub> may further be R<sub>8</sub><sup>+</sup>;

m is 0 or 1; and

R<sub>8</sub><sup>+</sup> is H<sup>+</sup> or a cation;

provided that:

(i) at least one of R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R'<sub>7</sub> is a hydrocarbon chain as defined in (a) above substituted by a negatively charged group or by an acidic group that is converted to a negatively charged group at the physiological pH; or

(ii) at least one of  $R_1$ ,  $R_2$ , and  $R_4$  is OH, SH,  $O^-R_8^+$  or  $S^-R_8^+$ ; or

(iii) at least one of  $R_1$ ,  $R_2$ , and  $R_4$  is OH, SH,  $O^-R_8^+$  or  $S^-R_8^+$  and at least one of  $R_5$ ,  $R_6$ ,  $R_7$  and  $R'_7$  is a hydrocarbon chain substituted by a negatively charged group or by an acidic group that is converted to a negatively charged group at the physiological pH; or

(iv) at least one of  $R_1$ ,  $R_2$ , and  $R_4$  is OH, SH,  $O^-R_8^+$  or  $S^-R_8^+$  and at least one of  $R_5$ ,  $R_6$ ,  $R_7$  and  $R'_7$  is a residue of an amino acid, a peptide or of a protein; or

(v) at least one of  $R_5$ ,  $R_6$ ,  $R_7$  and  $R'_7$  is a hydrocarbon chain substituted by a negatively charged group or by an acidic group that is converted to a negatively charged group at the physiological pH and at least one of  $R_5$ ,  $R_6$ ,  $R_7$  and  $R'_7$  is a residue of an amino acid, a peptide or of a protein;

wherein said negatively charged group is selected from the group consisting of  $COO^-$ ,  $COS^-$ ,  $SO_3^-$ , and  $PO_3^{2-}$  and said acidic group that is converted to a negatively charged group at the physiological pH is selected from the group consisting of COOH, COSH,  $SO_3H$ , and  $PO_3H_2$ ;

but excluding the compounds of formula I wherein M is as defined,  $R_3$  is  $-C(=O)CH_3$ ,  $R_1$  is OH or  $OR_8^+$  and  $R_2$  is  $-OCH_3$ , and the compound of formula II wherein M is 2H,  $R_3$  is  $-C(=O)CH_3$ ,  $R_1$ ,  $R_2$  and  $R_4$  are OH, and m is 0 or 1. ~~or both, excluding pentacyclie~~

~~bacteriochlorophyll derivatives having a free  $\text{CH}_2\text{CH}_2\text{COOH}$  or a  $\text{CH}_2\text{CH}_2\text{COO}^-$  group at position 17, and tetraacyelic bacteriochlorophyll derivatives devoid of a central metal atom and having a  $\text{CH}_2\text{CH}_2\text{COOH}$  group at position 17, a  $\text{CH}_2\text{COOH}$  or  $\text{COOH}$  group at position 15, a  $\text{COOH}$  group at position 13, methyl groups at the positions 2, 7, 12, 18, and ethyl groups at the positions 3 and 8.~~

2. (Currently Amended) A The bacteriochlorophyll derivative compound according to claim 1 containing two negatively charged groups.

3. (Currently Amended) A The bacteriochlorophyll derivative compound according to claim 1 containing three negatively charged groups.

4-9. (Cancelled)

10. (Currently Amended) A The bacteriochlorophyll derivative compound of the formula I or II according to claim 7-1, wherein  $\text{R}_1$  is  $\text{Y}-\text{R}_5$ ; Y is O, S or NH; and  $\text{R}_5$  is a hydrocarbon chain substituted by functional groups selected from of the group consisting of OH, SH,  $\text{SO}_3\text{H}$ ,  $\text{NH}_2$ ,  $\text{CONH}_2$ ,  $\text{COOH}$ ,  $\text{COSH}$ , and  $\text{PO}_3\text{H}_2$ .

11. (Currently Amended) A The bacteriochlorophyll  
derivative compound of the formula I or II according to claim ~~7-1~~,  
wherein  $R_5$  is the residue of an amino acid, a peptide or a  
protein.

12. (Currently Amended) A The bacteriochlorophyll  
derivative compound of the formula I or II according to claim ~~7~~ 1  
containing a central Pd metal atom.

13. (Currently Amended) A The bacteriochlorophyll  
derivative compound of the formula I according to claim ~~7~~ 1,  
wherein:

M is Pd;

$R_1$  is  $-\text{NH}-(\text{CH}_2)_n-\text{SO}_3^-\text{R}_8^+$ ,  $-\text{NH}-(\text{CH}_2)_n-\text{COO}^-\text{R}_8^+$ ;  $-\text{NH}-(\text{CH}_2)_n-\text{PO}_3^{2-}(\text{R}_8^+)_2$ ;

$R_2$  is methoxy;

$R_3$  is  $-\text{C}(=\text{O})-\text{CH}_3$ ;

$\text{R}_8^+$  is a monovalent cation such as  $\text{K}^+$ ,  $\text{Na}^+$ ,  $\text{Li}^+$ ,  $\text{NH}_4^+$ ; and

n is an integer from 1 to 10, ~~preferably 2 or 3.~~

14. (Currently Amended) A The bacteriochlorophyll  
derivative compound of the formula II according to claim ~~7~~ 1,  
wherein:

M represents 2H, divalent Pd, Cu, or Zn or trivalent Mn;

Appln. No. 10/534,692  
Amdt. dated January 25, 2010  
Reply to Office Action of September 24, 2009

$R_1$  is  $-O^-R_8^+$ ,  $-NH-(CH_2)_n-SO_3^-R_8^+$ ,  $-NH-(CH_2)_n-COO^-R_8^+$  or  $-NH-(CH_2)_n-PO_3^{2-}(R_8^+)_2$ ; or  $Y-R_5$ , wherein  $Y$  is O, S or NH and  $R_5$  is the residue of an amino acid, a peptide or a protein;

$R_2$  is  $C_1-C_6$  alkoxy, ~~preferably methoxy~~;

$R_3$  is  $-C(=O)-CH_3$ ,  $-CH=N-(CH_2)_n-SO_3^-R_8^+$ ;  $-CH=N-(CH_2)_n-COO^-R_8^+$ ;  $-CH=N-(CH_2)_n-PO_3^{2-}(R_8^+)_2$ ;  $-CH_2-NH-(CH_2)_n-SO_3^-R_8^+$ ;  $-CH_2-NH-(CH_2)_n-COO^-R_8^+$ ; or  $-CH_2-NH-(CH_2)_n-PO_3^{2-}(R_8^+)_2$ ;

$R_4$  is  $-NH-(CH_2)_n-SO_3^-R_8^+$ ;  $-NH-(CH_2)_n-COO^-R_8^+$ ; or  $-NH-(CH_2)_n-PO_3^{2-}(R_8^+)_2$ ;

$R_8^+$  is a monovalent cation, ~~preferably  $K^+$~~ ; and

$m$  is 1, and  $n$  is an integer from 1 to 10, ~~preferably 2 or 3~~.

**15. (Currently Amended)** ~~A~~ The bacteriochlorophyll  
derivative compound of formula II in claim 7 1 wherein:

$M$  is divalent Pd;

$R_1$  is  $-O^-R_8^+$ ,  $-NH-(CH_2)_n-SO_3^-R_8^+$ , or  $Y-R_5$ , wherein  $Y$  is O, S or NH and  $R_5$  is the residue of an amino acid, a peptide or a protein;

$R_2$  is  $C_1-C_6$  alkoxy, ~~preferably methoxy~~;

$R_3$  is  $-C(=O)-CH_3$ ,  $-CH=N-(CH_2)_n-SO_3^-R_8^+$ ; or  $-CH_2-NH-(CH_2)_n-SO_3^-R_8^+$ ;

$R_4$  is  $-NH-(CH_2)_n-SO_3^-R_8^+$ ;  $NH-(CH_2)_n-COO^-R_8^+$ ; or  $NH-(CH_2)_n-PO_3^{2-}(R_8^+)_2$ ;

$R_8^+$  is a monovalent cation, ~~preferably  $K^+$~~ ;

m is 1, and n is 2 or 3.

**16. (Currently Amended)** A-The bacteriochlorophyll derivative compound of the formula I according to claim 13, consisting of the compound Palladium bacteriopheophorbide a 17<sup>3</sup>-(3-sulfopropyl)amide potassium salt.

**17. (Currently Amended)** A-The bacteriochlorophyll derivative compound of the formula II according to claim 15, selected from the group consisting of:

Palladium 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl) amide dipotassium salt;

3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl) amide dipotassium salt;

Palladium 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>,17<sup>3</sup>-di(3-sulfopropyl)amide dipotassium salt;

Palladium 3<sup>1</sup>-(3-sulfopropylimino)-15-methoxycarbonylmethyl-rhodobacterio-chlorin 13<sup>1</sup>,17<sup>3</sup>-di(3-sulfopropyl)amide tripotassium salt;

Copper(II) 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl) amide dipotassium salt;

Zinc 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl) amide dipotassium salt;

Appln. No. 10/534,692  
Amdt. dated January 25, 2010  
Reply to Office Action of September 24, 2009

Manganese(III) 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-  
rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl)amide dipotassium salt;

Palladium 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-  
rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl) amide, 17<sup>3</sup>-(N-  
immunoglobulin G) amide potassium salt;

Palladium 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-  
rhodobacteriochlorin 13<sup>1</sup>-(2-carboxy-ethyl)amide dipotassium salt;

Palladium 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-  
rhodobacteriochlorin 13<sup>1</sup>-(3-phosphopropyl)amide tripotassium  
salt; and

Palladium 3<sup>1</sup>-(3-sulfopropylamino)-15-methoxycarbonylmethyl-  
rhodobacte-riochlorin 13<sup>1</sup>,17<sup>3</sup>-di(3-sulfopropyl)amide tripotassium  
salt.

18. (Original) Palladium 3<sup>1</sup>-oxo-15-  
methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl)  
amide dipotassium salt.

19. (Currently Amended) A pharmaceutical composition  
comprising a the bacteriochlorophyll derivative compound according  
to claim 1, and a pharmaceutically acceptable carrier.

20-35. (Cancelled)



**36. (Currently Amended)** A method for vascular-targeted  
~~tumor~~ photodynamic therapy (VTP), which comprises:

- (a) administering to an individual in need a the  
bacteriochlorophyll compound according to claim 1; and
- (b) irradiating the local area of the tumor.

**37. (Currently Amended)** A method for photodynamic  
therapy of age-related macular degeneration by vascular  
occlusion, which comprises:

- (a) administering to an individual in need a the  
bacteriochlorophyll compound according to claim 1; and
- (b) irradiating the local area of the macular degeneration.

**38. (Currently Amended)** A method for tumor diagnosis  
which comprises:

- (a) administering to a subject suspected of having a tumor,  
a the bacteriochlorophyll compound according to claim 1; and
- (b) irradiating the subject by standard procedures and  
measuring the fluorescence of the suspected area, wherein a  
higher fluorescence indicates tumor sites.

**39-41 (Cancelled).**

**42. (Currently Amended)** ~~The A~~ compound Palladium bacteriopheophorbide a 17<sup>3</sup>-(3-sulfo-1-oxysuccinimide) ester sodium salt, ~~as an intermediate.~~

**43. (Currently Amended)** A method for the preparation of compounds of formula II ~~in~~ of claim 7 1, wherein R<sub>1</sub> is -O<sup>-</sup> R<sub>8</sub><sup>+</sup>; R<sub>2</sub> is -OCH<sub>3</sub>; R<sub>3</sub> is acetyl; R<sub>4</sub> is a group -NH-(CH<sub>2</sub>)<sub>n</sub>-SO<sub>3</sub><sup>-</sup>R<sub>8</sub><sup>+</sup>; R<sub>8</sub><sup>+</sup> is a monovalent cation; m is 1 and n is 1 to 10, which comprises:

(i) reacting the corresponding M-bacteriopheophorbide of formula I, wherein R<sub>1</sub> is OH with an aminosulfonic acid of the formula H<sub>2</sub>N-(CH<sub>2</sub>)<sub>n</sub>-SO<sub>3</sub>H in a R<sub>8</sub><sup>+</sup>-buffer; and

(ii) isolating the desired compound of formula II.

**44. (Currently Amended)** The method according to claim 43 for preparation of palladium 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl) amide dipotassium salt, which comprises: (i) reacting Pd-bacteriopheophorbide a with taurine of the formula H<sub>2</sub>N-(CH<sub>2</sub>)<sub>2</sub>-SO<sub>3</sub>H in a K<sup>+</sup> -buffer; and (ii) isolating the ~~title~~ compound.

**45. (Currently Amended)** A method for the preparation of compounds of formula II in claim 7 1, wherein R<sub>1</sub> is -O<sup>-</sup> R<sub>8</sub><sup>+</sup>; R<sub>2</sub> is -OCH<sub>3</sub>; R<sub>3</sub> is acetyl; R<sub>4</sub> is a group -NH-(CH<sub>2</sub>)<sub>n</sub>-COO<sup>-</sup> R<sub>8</sub><sup>+</sup>; R<sub>8</sub><sup>+</sup> is a monovalent cation; m is 1 and n is 1 to 10, which comprises:

Appln. No. 10/534,692  
Amdt. dated January 25, 2010  
Reply to Office Action of September 24, 2009

(i) reacting the corresponding M-bacteriopheophorbide of formula I wherein  $R_1$  is OH with an aminocarboxylic acid of the formula  $H_2N-(CH_2)_n-COOH$  in a  $R_8^+$ -buffer; and

(ii) isolating the desired compound of formula II.

**46. (Currently Amended)** A method for the preparation of compounds of formula II in claim 7 1, wherein  $R_1$  is  $-O^- R_8^+$ ;  $R_2$  is  $-OCH_3$ ;  $R_3$  is acetyl;  $R_4$  is a group  $-NH-(CH_2)_n-PO_3^{2-} (R_8^+)_2$ ;  $R_8^+$  is a monovalent cation; m is 1 and n is 1 to 10, which comprises:

(i) reacting the corresponding M-bacteriopheophorbide of formula I wherein  $R_1$  is OH with an aminophosphonic acid of the formula  $H_2N-(CH_2)_n-PO_3H_2$  in a  $R_8$ -buffer; and

(ii) isolating the desired compound of formula II.

**47. (Currently Amended)** A method for the preparation of compounds of formula II in claim 7 1, wherein  $R_1$  and  $R_4$  contain the same negatively charged group, which comprises:

(i) reacting the corresponding M-bacteriopheophorbide with an excess of the aminosulfonic, aminocarboxylic or aminophosphonic acid in a  $R_8^+$ -buffer; and

(ii) isolating the desired 13,17-disubstituted derivative compound of formula II.

**48. (Currently Amended)** A method for the preparation of compounds of formula II in claim 7 1, wherein  $R_1$  and  $R_4$  are each a group  $-NH-(CH_2)_n-SO_3^-R_8^+$ ;  $R_2$  is  $-OCH_3$ ;  $R_3$  is acetyl;  $R_8^+$  is a monovalent cation;  $m$  is 1 and  $n$  is 1 to 10, which comprises:

(i) coupling the corresponding M-bacteriopheophorbide of formula I wherein  $R_1$  is OH with N-hydroxy-sulfosuccinimide (sulfo NHS) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC);

(ii) reacting the resulting M-bacteriopheophorbide-17<sup>3</sup>-N-hydroxy-sulfosuccinimide ester with an excess of an aminosulfonic acid of the formula  $H_2N-(CH_2)_n-SO_3H$  in a  $R_8^+$ -buffer, thus obtaining a compound of formula I having a sole negatively charged group at position 17;

(iii) reacting the product of step (ii) with an excess of  $H_2N-(CH_2)_n-SO_3H$  in a  $R_8^+$ -buffer; and

(iv) isolating the desired compound of formula II.

**49. (Currently Amended)** A method for the preparation of compounds of formula II in claim 7 1, wherein  $R_1$  and  $R_4$  are each a group  $-NH-(CH_2)_n-COO^-R_8^+$ ;  $R_2$  is  $-OCH_3$ ;  $R_3$  is acetyl;  $R_8^+$  is a monovalent cation;  $m$  is 1 and  $n$  is 1 to 10, which comprises:

(i) coupling the corresponding M-bacteriopheophorbide of formula I wherein  $R_1$  is OH with N-hydroxy-sulfosuccinimide (sulfo

NHS) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC);

(ii) reacting the resulting M-bacteriopheophorbide-17<sup>3</sup>-N-hydroxy-sulfosuccinimide ester with an excess of an aminocarboxylic acid of the formula  $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{COOH}$  in a  $\text{R}_8^+$ -buffer, thus obtaining a compound of formula I having a sole negatively charged group at position 17;

(iii) reacting the product of step (ii) with an excess of  $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{COOH}$  in a  $\text{R}_8^+$ -buffer; and (iv) isolating the desired compound of formula II.

**50. (Currently Amended)** A method for the preparation of compounds of formula II in claim 7 1, wherein  $\text{R}_1$  and  $\text{R}_4$  are each a group  $-\text{NH}-(\text{CH}_2)_n-\text{PO}_3^{2-} \text{R}_8^+$ ;  $\text{R}_2$  is  $-\text{OCH}_3$ ;  $\text{R}_3$  is acetyl;  $\text{R}_8^+$  is a monovalent cation; m is 1 and n is 1 to 10, which comprises:

(i) coupling the corresponding M-bacteriopheophorbide of formula I wherein  $\text{R}_1$  is OH with N-hydroxy-sulfosuccinimide (sulfo NHS) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC);

(ii) reacting the resulting M-bacteriopheophorbide-17<sup>3</sup>-N-hydroxy-sulfosuccinimide ester with an excess of an aminophosphonic acid of the formula  $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{PO}_3\text{H}_2$  in a  $\text{R}_8^+$ -buffer, thus obtaining a compound of formula I having a sole negatively charged group at position 17;

Appln. No. 10/534,692

Amdt. dated January 25, 2010

Reply to Office Action of September 24, 2009

(iii) reacting the product of step (ii) with an excess of  $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{PO}_3\text{H}_2$  in a  $\text{R}_8^+$ -buffer; and (iv) isolating the desired compound of formula II.